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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/978,498	10/15/2001	Adrian Clausell	2055-181	4848

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EXAMINER	
PRATS, FRANCISCO CHANDLER	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 02/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/978,498	CLAUSELL ET AL.	
	Examiner	Art Unit	
	Francisco C Prats	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-14,16-20 and 23-55* is/are pending in the application.

4a) Of the above claim(s) *23-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-14,16-20 and 23-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed December 15, 2003, has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 5-14, 16-20 and 23-55 are pending.

As a matter of clarification, note that applicant's current response lists claims 1-4 and 56-95 as being "withdrawn", suggesting that those claims are pending but non-examined. However, applicant clearly cancelled those claims on page 3 of the paper filed May 21, 2003. ("Please ***cancel*** claims 1-4, and 56-95, without prejudice or disclaimer, as directed to non-elected inventions.") (Emphasis added.) Claims 1-4 and 56-95 are therefore in fact cancelled, and therefore not pending.

Election/Restrictions

Claims 23-37 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species of invention, there being no allowable generic or linking claim. As discussed in the previous office action, election was made **without** traverse in Paper No. 8 filed May 21, 2003.

Claims 5-14, 16-20 and 38-55 are examined on the merits to the extent they read on the elected species (caspase, glycerol, rhodamine 110), as well as the use of DMSO as an uptake-enhancing agent for intact cell enzyme assays.

Claim Rejections - 35 USC § 112

Claims 9, 10, 54 and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is confusing, and therefore indefinite, because it requires the substrate/analyte to be mixed with the uptake-enhancing agent. The confusion lies in the fact that claim 9 depends from claim 1, which states that the incubation of substrate/analyte takes place "in the presence of an agent that enhances uptake of said substrate or analyte [.]" Thus, it is confusing what is encompassed by claim 9, since claim 1 already requires the substrate/analyte and uptake-enhancing agent to be mixed. Because claim 54 contains the same limitation as claim 9, and ultimately depends from claim 1, claim 54 is indefinite for the same reasons as claim 9.

Claim 10 is confusing, and therefore indefinite, because claim 10 requires the substrate or analyte to not be mixed with

the uptake-enhancing agent during incubation. The confusion lies in the fact that claim 10 depends from claim 1, and claim 1 states that the incubation of substrate/analyte takes place "in the presence of an agent that enhances uptake of said substrate or analyte [.]" Thus, claim 10 cannot logically depend from claim 1 because claim 10 excludes a limitation explicitly required by claim 1. Moreover, it is unclear how the claimed process can possibly be performed without mixing the ingredients required for the assay. That is, as claimed, claim 10 appears to be a physical impossibility. Claim 55, which ultimately depends from claim 1, also excludes the mixing of the various ingredients, despite claim 1's requirement of incubation together. A holding of indefiniteness over the cited claims is clearly required.

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. Applicant points to page 47, lines 17-22, of the specification to clarify the difference between "mixed" and "unmixed" samples. However, that portion of the specification reads as follows:

> invention, unless specified.
>
> Having now generally described the invention, the same will be more readily understood through reference to the following examples, which are provided by way of illustration, and are not

intended to be limiting of the present invention, unless specified.

Example 1

Thus, that section of the specification provides little help in remedying the lack of clarity in the claims with respect to what applicant means by "mixed" and "not mixed." Similarly, the drawing legends do little to clarify what the claims actually mean by those terms.

With all due respect, once both reagents are added to the culture medium, they are both present in the culture medium, and therefore they have been "mixed" for all practical purposes, as any reasonable practitioner would construe that term. It is entirely confusing how these *already* "mixed" reagents could require an *additional* limitation stating that the reagents are "mixed", as recited in claim 9. Moreover, it is entirely confusing how the same assay could be performed when these reagents are "not mixed", as recited in claim 10. This confusion with respect to the actual steps required for practicing the claimed process requires a holding of indefiniteness.

Further still, construing the claims to encompass the mere "co-presence" of the solubilizing agent and indicator reagent,

as urged by applicant, would be unreasonable. Such a construction would merely require that the assay be run in the presence of the solubilizing agent. Thus, any laboratory performing the assay could be considered an infringer merely by having the solubilizing agent on the shelf, even if the solubilizing agent were never added to the reaction milieu. Moreover, construing the claim at its broadest, "co-presence" merely requires coexistence, without regard to physical proximity. This extremely broad construction would enormously broaden the scope of prior art applicable to the claims, and is therefore not reasonable.

In sum, because the exact process steps used to perform the assays are not written out with any particularity, the Examples in the specification do not clarify, or state, what is meant by "mixed" and "not mixed." The specification does not state with particularity what was added to what, and when this addition was performed. It does appear that it may be applicant's intention to encompass situations where the solubilizing reagent and indicator reagent were either (a) mixed before addition to the culture medium, or (b) added to the culture medium separately, without mixing beforehand. However, in view of the lack of specific disclosure in this regard, it is not clear that this is what was done, or that the application as filed has support for

such claim language. Therefore, for the reasons above, the rejection must be maintained.

Claim Rejections - 35 USC § 102

Claims 5, 9 and 16-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Wansink et al (J. Cell Biol. 122(2):283-293 (1993)).

Wansink et al disclose a process whereby incorporation of BrUTP into RNA is measured over time in permeabilized human bladder carcinoma cells. See Fig. 1, page 285. The cells were permeabilized using a buffer comprising 25% glycerol, the elected species of uptake-enhancing agent. See page 284, left hand column, section entitled *"BrUTP Incorporation in Permeabilized Cells (Run-on Transcription)"*, subsection entitled *"Cells in Suspension."* A holding of anticipation of the cited claims is clearly required.

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. The anticipation rejection over the Los reference has been withdrawn because digitonin is not one of the permeabilizing/solubilizing agents recited in the claims as amended. The anticipation rejection over the Lucas and Zhang references has been withdrawn because the concentrations of DMSO

described in those references is not the same as the concentration of DMSO required in the claims as amended.

However, the anticipation rejection over the Wansink reference is maintained because the new language "assaying said metabolically active whole cell" does not exclude the situation presented in Wansink. Specifically, although the Wansink assay results in cell killing, the assay itself is performed on metabolically active whole cells, as evidenced by the fact that the cells are maintained intact, and transcription continues to occur. Note that the new claim language does not require the cells to remain intact after assaying. The new claim language merely requires that metabolically active whole cells be assayed. Because, contrary to applicant's argument, the new claim language is sufficiently broad to encompass the situation described by Wansink, the anticipation rejection must be maintained.

Claim Rejections - 35 USC § 103

Claims 5, 11, 12 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lucas et al (U.S. Pat. 5,698,411).

Lucas discloses the use of the derivates of elected species of indicator moiety, rhodamine 110, in assays of whole cell enzyme activity. Lucas discloses that additional agents, such

as DMSO, preferably at 5%, may be used to assist the transfer of the assay compounds into cells. See column 29, line 61 through column 30, line 40. Lucas differs from the claimed subject matter in failing to explicitly disclose a single embodiment combining the uptake-enhancing agent with multiple enzyme assays, either simultaneous or sequential, as recited in claims 11 and 12, or the use of 20 to 60% DMSO as the solubilizing agent, as recited in claim 5 as amended.

However, Lucas clearly discloses that adequate analysis of the disease states of cells requires multiple enzyme assays, with the generation of a specific data matrix for a number of different enzymes. See discussion at columns 43-48. The artisan of ordinary skill, recognizing that the enzyme assays would have been suitably performed either sequentially or simultaneously, clearly would have been motivated to have performed the assays using either tactic, reasonably expecting to generate the required data set. Thus, the claimed combination of uptake-enhancing agent with multiple enzyme assays clearly would have been obvious in view of Lucas' disclosure, the artisan of ordinary skill recognizing the advantages of solubility agents as disclosed by Lucas, and also recognizing the suitability of multiple enzyme assays to generate the data set disclosed by Lucas as being required for

accurate disease diagnosis. A holding of obviousness over claims 11 and 12 is therefore required.

As to the amount of DMSO recited in claim 22, note specifically that Lucas clearly discloses that suitable amounts of solubilizing agent can be determined by optimization. See column 30, lines 13 and 14 ("The effective amount of solubilizing component may be empirically determined . . . ."). Because Lucas considers the concentration of solubilizing component to be a result-effective parameter which can be routinely optimized, the claimed concentration of DMSO must be considered obvious absent some demonstration that said concentration confers an unexpected result upon the claimed subject matter. A holding of obviousness is therefore required over claim 22.

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. The holding of obviousness is not based on what the prior art suggests might be nice, but rather on the fact that the reference directly discloses that disease states are often characterized by aberrations in more than one enzyme activity. Given this fact, and the fact that the reference provides a very comprehensive list of assayable enzymes suitable for diagnosing disease states, the prior art clearly provides motivation for

conducting multiple enzyme assays, either sequentially or simultaneously, so as to diagnose those disease states requiring multiple enzyme assays. Moreover, in view of the fact that applicant's disclosure is substantially less explicit than Lucas' with respect to the specifics of the methodology and rationale for conducting multiple enzyme assays sequentially and/or simultaneously, applicant's argument could well be taken as an argument that their own disclosure does not sufficiently support the claim language as presented.

As to the use of higher amounts of DMSO recited in the claims as amended, note specifically, as stated above, that suitable amounts of solubilizer would have been readily determined through routine experimentation. While applicant points to the Lucas reference's discussion about problems with higher concentrations of solubilizers, applicant's argument fails to point out that Lucas provides methods for solving this problem. See column 30, lines 55, et seq., discussing how the problem of cellular expulsion can be solved by adding other ingredients.

Lastly, as to the assertion of unexpected results, note that the assays in the specification were conducted using only one cell line, and one indicator compound under specific conditions. Applicant's claims are much broader than the

alleged showing of unexpected results. Thus, the alleged showing of unexpected result is not commensurate in scope with the subject matter presently claimed. The rejection must therefore be maintained.

Claims 5-14, 20 and 38-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Landrum et al (U.S. Pat. 5,976,822) in view of Lucas et al (U.S. Pat. 5,698,411).

Landrum discloses the use of derivates of the elected species of indicator moiety, rhodamine 110, in assays of whole cell enzyme activity, including caspase activity, for the purpose of ascertaining apoptotic cells, as well as for the purpose of distinguishing apoptotic cells from necrotic cells. See Example 10, at column 22, line 34 through column. See also, abstract. Note specifically the use of different substrate moieties for different enzymes, disclosed at Table 1, column 22, lines 1-19. Landrum differs from the claims in that Landrum does not disclose the use of uptake-enhancing agents in the assays.

However, Landrum clearly discloses that additional ingredients, including "solubilizing components" can be used to improve the assays conducted according to the disclosure therein. See column 10, lines 21-37. Moreover, Lucas clearly

discloses that intact cell enzyme assays using rhodamine 110 derivatives can benefit from the addition of solubilizing agents which allow the assay compound to pass into the cell. See column 29, line 61 through column 30, line 40. Thus, the artisan of ordinary skill at the time of applicant's invention clearly would have recognized from Lucas the advantages of solubilizing agents in assays using rhodamine 110 derivatives as assay compounds. The artisan of ordinary skill would therefore have been motivated to have used Lucas' solubilizing compounds in the caspase assays of Landrum which also use rhodamine 110 as the assay compound, thereby assisting in the transfer of the assay compound into the intact cells, as disclosed by Lucas. A holding of obviousness over the cited claims is therefore required.

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. Applicant urges that because certain of Lucas' dyeing agents are toxic to the cell that Lucas cannot teach assaying a metabolically active whole cell as recited in the claims as amended. Applicant's argument ignores the entire point of the Lucas disclosure. The title of the Lucas patent is:

"Method for determining activity of enzymes ***in metabolically active whole cells"*** (emphasis added).

Similarly, the first sentence of the abstracts states: "A method for assaying the activity of an enzyme ***inside a metabolically active whole cell*** is disclosed." (Emphasis added.) Thus, because it would be antithetical to the entire disclosure, one of ordinary skill in the art would not read the use of supposedly toxic compounds by Lucas as rendering the cells inactive, as urged by applicant. Rather, as is clear from the disclosure of the reference, the entire point of the disclosed assays is to perform them on metabolically active cells.

As to the reiterated argument regarding the unexpected results note that the assays in the specification were conducted using only one cell line, and one indicator compound under specific conditions. Applicant's claims are much broader than the alleged showing of unexpected results. Thus, the alleged showing of unexpected result is not commensurate in scope with the subject matter presently claimed. The rejection must therefore be maintained.

Claims 5-14, 20 and 38-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al (U.S. Pat. 6,248,904 B1).

As discussed above, Zhang discloses the use of derivates of the elected species of indicator moiety, rhodamine 110, in assays of whole cell enzyme activity, including caspase activity, for the purpose of ascertaining apoptotic as well as anticancer efficacy of therapeutic agents. As also discussed above, Zhang discloses that additional solubilizing agents, such as DMSO, as well as liposomes or detergents, may be used to assist the transfer of the assay compounds into cells, and that Zhang is therefore considered to anticipate claims 5-9, 13-15, 38-40, 46, 48-51 and 54.

Zhang differs from claims 11, 12, 41 and 42 in failing to explicitly disclose a single embodiment combining the uptake-enhancing agent with multiple enzyme assays, either simultaneous or sequential, as recited in claims 11, 12, 41 and 42, or the use of 20 to 60% DMSO as the solubilizing agent, as recited in claims 20-22.

However, Zhang clearly discloses that different disease states can be assayed using different enzyme assays. See discussion at column 5, line 4 through column 6, line 15. The artisan of ordinary skill, recognizing that the enzyme assays for disease diagnosis would have been suitably performed either sequentially or simultaneously, clearly would have been motivated to have performed the assays using either tactic,

reasonably expecting to generate the disease diagnosis regardless of whether the assays were performed at the same time, or one after the other. Thus, the claimed combination of uptake-enhancing agent with multiple enzyme assays clearly would have been obvious in view of Zhang's disclosure, the artisan of ordinary skill recognizing the advantages of solubility agents as disclosed by Zhang's, and also recognizing the suitability of multiple enzyme assays to generate the data set disclosed by Zhang as being required for accurate disease diagnosis. A holding of obviousness over claims 11, 12, 41 and 42 is therefore required.

As to the amount of DMSO recited in claims 20-22, note specifically that Lucas clearly discloses that the artisan of ordinary skill would have recognized that using differing concentrations of solubilizing component would have resulted in different results. Thus, the artisan of ordinary skill would have considered the concentration of solubilizing component to be a result-effective parameter which would have been routinely optimized. The claimed concentration of DMSO must be considered obvious absent some demonstration that said concentration confers an unexpected result upon the claimed subject matter. A holding of obviousness is therefore required over claims 20-22.

Further still, assays of intensity or magnitude over time were well known in the art at the time of applicant's invention. Absent some demonstration that these assays perform in a manner unexpected in view of the prior art, a holding of obviousness over the cited claims is clearly required.

In sum, because the prior art fairly suggests the claimed subject matter, a holding of obviousness is clearly required.

All of applicant's argument regarding this ground of rejection has been fully considered but is not persuasive of error. The differences between the prior art and the claims have been noted. As to the failure of Zhang to disclosure multiple enzyme assays, as discussed above, Zhang clearly discloses that different disease states can be assayed using different enzyme assays. See discussion at column 5, line 4 through column 6, line 15. The artisan of ordinary skill, recognizing that the enzyme assays for disease diagnosis would have been suitably performed either sequentially or simultaneously, clearly would have been motivated to have performed the assays using either tactic, reasonably expecting to generate the disease diagnosis regardless of whether the assays were performed at the same time, or one after the other. Thus, the claimed combination of uptake-enhancing agent with multiple enzyme assays clearly would have been obvious in view

of Zhang's disclosure, the artisan of ordinary skill recognizing the advantages of solubility agents as disclosed by Zhang's, and also recognizing the suitability of multiple enzyme assays to generate the data set disclosed by Zhang as being required for accurate disease diagnosis.

As to the failure of the reference to disclose the use of 20 to 60% DMSO, note specifically that suitable amounts or concentrations of solubilizing/permeabilizing agent would have been readily determined by the artisan of ordinary skill through routine experimentation.

As to the failure of the reference to suggest the use of glycerol, note that claim 5 only recites the use of glycerol in the alternative. Thus, Zhang is properly held to render the cited claims obvious because solubilizing agents other than glycerol, e.g. DMSO, whose concentration would have been determined by routine experimentation, are clearly disclosed by Zhang as being suitable in the disclosed assays. Lastly, note that at the time the previous action was issued, independent claim 5 did not recite the use of glycerol as a permeabilizing agent.

Lastly, with respect to the assertions regarding unexpected results, note that applicant has presented results with respect to only one assay, whereas the claims encompass numerous assays

having different reagents and process conditions than the reagents and conditions in applicant's single assay. Clearly, the assertion of unexpected result

Claims 5-14, 16-20 and 38-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Landrum et al (U.S. Pat. 5,976,822) in view of Lucas et al (U.S. Pat. 5,698,411), as applied to claims 5-14, 20 and 38-54 above, and in further view of Wansink et al (J. Cell Biol. 122(2):283-293 (1993)).

As amended, independent claim 5 now requires the use of glycerol one of the alternatively named permeabilizing components. Thus, because of the present amendment, the claims under examination now positively recite embodiments requiring the use of glycerol as a permeabilizing agent in caspase assays, in assays using rhodamine 110, and in caspase assays using rhodamine 110. As discussed above with respect to Landrum and Lucas, these references suggest the use of permeabilizing agents such as DMSO for the purpose of allowing an assay indicator compound to enter the cell in whole-cell enzyme assays. Neither Landrum nor Lucas disclose the use of glycerol as the permeabilizing agent.

However, Wansink et al disclose a process whereby incorporation of BrUTP into RNA is measured over time in permeabilized human bladder carcinoma cells. See Fig. 1, page

285. The cells were permeabilized using a buffer comprising 25% glycerol, the elected species of uptake-enhancing agent. See page 284, left hand column, section entitled "*BrUTP Incorporation in Permeabilized Cells (Run-on Transcription)*", subsection entitled "*Cells in Suspension.*" Thus, the artisan of ordinary skill, recognizing from Wansink that 25% glycerol was a permeabilizing agent suitable for allowing entry of indicator compounds into intact cells for whole-cell assays, clearly would have been motivated to have used said glycerol in the assays disclosed by Landrum and/or Lucas. A holding of obviousness of the cited claims is clearly required.

Claims 5-14, 16-20 and 38-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al (U.S. Pat. 6,248,904 B1), as applied to claims 5-14, 20 and 38-54 above, and in further view of Wansink et al (J. Cell Biol. 122(2):283-293 (1993)).

As amended, independent claim 5 now requires the use of glycerol one of the alternatively named permeabilizing components. Thus, because of the present amendment, the claims under examination now positively recite embodiments requiring the use of glycerol as a permeabilizing agent in caspase assays, in assays using rhodamine 110, and in caspase assays using

rhodamine 110. As discussed above with respect to Zhang, that reference suggests the use of permeabilizing agents such as DMSO for the purpose of allowing an assay indicator compound to enter the cell in whole-cell enzyme assays. Zhang does not disclose the use of glycerol as the permeabilizing agent.

However, Wansink et al disclose a process whereby incorporation of BrUTP into RNA is measured over time in permeabilized human bladder carcinoma cells. See Fig. 1, page 285. The cells were permeabilized using a buffer comprising 25% glycerol, the elected species of uptake-enhancing agent. See page 284, left hand column, section entitled "*BrUTP Incorporation in Permeabilized Cells (Run-on Transcription)*", subsection entitled "*Cells in Suspension.*" Thus, the artisan of ordinary skill, recognizing from Wansink that 25% glycerol was a permeabilizing agent suitable for allowing entry of indicator compounds into intact cells for whole-cell assays, clearly would have been motivated to have used said glycerol in the assays disclosed by Zhang. A holding of obviousness of the cited claims is clearly required.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 571-272-0921. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Wityshyn can

be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Francisco C Prats
Primary Examiner
Art Unit 1651

FCP